27. A method for diagnosing a condition selected from the group consisting of susceptibility to normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage, and miscarriage-related infertility, comprising the steps of:

a) obtaining a fluid or tissue sample from at least one member selected from the group consisting of a female, a male, and a fetus;

b) detecting at least one HLA-G or HLA-G linked polymorphism in the sample; and

c) comparing the at least one HLA-G or HLA-G linked polymorphism in the sample to at least one HLA-G or HLA-G linked polymorphism associated with a condition selected from a normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage, and miscarriage-related infertility;

wherein the presence of an HLA-G or HLA-G linked polymorphism associated with a condition selected from a normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage, and miscarriage-related infertility in the sample is diagnostic for the selected condition.

28. The method of claim 27, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises detecting HLA-G or HLA-G linked nucleic acid.

29. The method of claim 28, wherein the HLA-G or HLA-G linked nucleic acid comprises DNA.

30. The method of claim 28, wherein the HLA-G or HLA-G linked nucleic acid comprises mRNA.

31. The method of claim 30, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises determining the size of the HLA-G or HLA-G linked mRNA.

32. The method of claim 30, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises determining the level of the HLA-G or HLA-G linked mRNA.

33. The method of claim 28, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises determining the sequence of all or part of the HLA-G or HLA-G linked nucleic acid.

34. The method of claim 29, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises determining the sequence of all or part of the HLA-G or HLA-G linked nucleic acid.

35. The method of claim 30, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises determining the sequence of all or part of the HLA-G or HLA-G linked nucleic acid.

36. The method of claim 28, wherein the HLA-G nucleic acid is analyzed for one or more of:

(a) the C allele or the T allele of codon 93 in exon 3; or

(b) the insertion allele or the deletion allele of exon 8.

37. The method of claim 33-35, wherein the effect of one or more of the HLA-G sequence variants on the size of all or part of the HLA-G mRNA is measured.

38. The method of claim 33-35, wherein the effect of one or more of the HLA-G sequence variants on the level of HLA-G mRNA is measured.

39. The method of claim 27, wherein all or part of the HLA-G sequence or HLA-G linked sequence is amplified.

40. The method of claim 39, wherein the amplification is achieved using at least one method selected from the group consisting of polymerase chain reaction, nucleic acid sequence based amplification, self sustained sequence replication, transcription-mediated amplification, strand displacement amplification, and ligase chain reaction.

41. The method of claim 27, wherein the step of comparing is performed by a method selected from the group consisting of association, linkage analysis, and transmission analysis.

42. The method of claim 27, wherein all or part of the HLA-G sequence is cloned into a vector.

43. The method of claim 27, wherein all or part of the nucleic acid sequence is determined using at least one method selected from the group consisting of DNA sequencing, glycosylase mediated polymorphism detection, restriction fragment length polymorphism analysis, enzymatic cleavage analysis, chemical cleavage analysis, hybridization to DNA probes, hybridization to RNA probes, hybridization to DNA probe arrays, hybridization to allele specific DNA probes, hybridization to allele-specific RNA probes, allele specific amplification analysis, electrophoretic mobility analysis, and 5' nuclease assay analysis.

44. The method of claim 27, wherein all or part of the HLA-G nucleic acid is expressed as a polypeptide using an expression system selected from the group consisting of in vitro transcription/translation, a prokaryotic cell, and a eukaryotic cell.

45. The method of claim 27, wherein the step of detecting the HLA-G or HLA-G linked polymorphism in the sample comprises detecting variant forms of all or part of at least one HLA-G protein or protein encoded by an HLA-G linked gene.

46. The method of claim 45, wherein detecting variant forms of all or part of at least one HLA-G protein or protein encoded by an HLA-G linked gene in the sample comprises determining the size of the HLA-G protein or protein encoded by an HLA-G linked gene.

47. The method of claim 45, wherein detecting variant forms of all or part of at least one HLA-G protein or protein encoded by an HLA-G linked gene in the sample comprises determining the level of the HLA-G protein or protein encoded by an HLA-G linked gene.

48. The method of claim 45, wherein the step of detecting variant forms of all or part of at least one HLA-G protein or protein encoded by an HLA-G linked gene comprises measuring the functional activity of all or part of the HLA-G protein or protein encoded by an HLA-G linked gene.

49. The method of claim 48, wherein measuring the functional activity of all or part of the HLA-G protein or protein encoded by an HLA-G linked gene comprises quantifying cells whose concentration changes as a result of HLA-G action.

50. The method of claim 48, wherein measuring the functional activity of all or part of the HLA-G protein or protein encoded by an HLA-G linked gene comprises quantifying molecules whose concentration changes as a result of HLA-G action.

51. The method of claim 48, wherein the effect of one or more of the HLA-G sequence variants on the functional activity of HLA-G is measured.

52. The method of claim 48, wherein the effect of one or more of the HLA-G sequence variants on the size of all or part of the HLA-G protein is measured.

53. The method of claim 48, wherein the effect of one or more of the HLA-G sequence variants on the level of HLA-G protein is measured.

54. The method of claim 49, wherein the cells are selected from the group consisting of blood mononuclear cells, T cells, natural killer cells, and HLA-G expressing cells.

55. The method of claim 48, wherein the functional activity of HLA-G is measured by measuring the peptide binding capability of all or part of HLA-G or variants thereof.

56. The method of claim 48, wherein the functional activity of HLA-G is measured by measuring the binding capability of all or part of the HLA-G or variants thereof to an HLA-G receptor.

57. The method of claim 48, wherein the functional activity of HLA-G is measured by measuring the expression levels of one ore more genes or proteins in HLA-G expressing cells.

58. The method of claim 48, wherein the function activity of HLA-G is measured by measuring the interaction of HLA-G or variants thereof with blood mononuclear cells or a subset thereof.

59. The method of claim 58, wherein the interaction of HLA-G or variants thereof with blood mononuclear cells or a subset thereof is measured by assessing at least one parameter selected from the group consisting of: cell proliferation, transformation, cytotoxic response, surface marker expression, cytokine production, conjugate formation, and target specificity.

60. The method of claim 45, wherein the HLA-G protein is partially or fully purified from a cell expressing HLA-G.

61. The method of claim 45, wherein the HLA-G is detected by immunoassay using one or more antibodies specific for HLA-G or variants thereof.

62. The method of claim 45, wherein all or part of the HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, and HLA-H genes are analyzed in one member selected from the group consisting of a female, a male, and a fetus.

63. The method of claim 50, wherein the molecules are selected from the group consisting of IL-1 beta, IL-2, IL-3, IL-4, IL-6, IL-10, and tumor necrosis factor-alpha, cytokeratins, pregnancy specific clycoprotein 1, human chorionic gonadotropin, and human placental lactogen.

64. The method of claim 27, wherein nucleic acid is measured using at least one method selected from the group consisting of:

(a) hybridization between cDNA from the cells and DNA probes;
(b) hybridization between cDNA from the cells and RNA probes;
(c) hybridization between cDNA from the cells and nucleic acid probe arrays;
(d) hybridization between RNA from the cells and DNA probes;
(e) hybridization between RNA from the cells and RNA probes;
(f) hybridization between RNA from the cells and nucleic acid probe arrays;
(g) quantitative amplification methods;
(h) reverse transcriptase polymerase chain reaction (RT-PCR);
(i) 5' nuclease assay;
(j) ribonuclease protection assay; and
(k) S1 nuclease assay.

65. The method of claim 45, wherein protein is measured using at least one method selected from the group consisting of:

(a) one dimensional gel electrophoresis and staining of proteins;
(b) two dimensional gel electrophoresis and staining of proteins;
(c) enzyme-linked immunosorbent assay (ELISA);
(d) radioimmunoassay (RIA);
(e) protein truncation test (PTT);
(f) immunoradiometric assay (IRMA);
g) immunozenzymatic assay (IEMA);
h) sandwich assay;
i) Western blotting using monoclonal antibodies; and
j) Western blotting using polyclonal antibodies.

66. A test kit for diagnosis of pre-eclampsia, eclampsia, intrauterine growth retardation, susceptibility to miscarriage, susceptibility to miscarriage-related infertility, and for monitoring progress of pregnancy.

67. The test kit of claim 66, wherein the test kit comprises nucleic acid sequences as identified by any one of SEQ ID NOS: 1 to 21.

68. The test kit of claim 67, wherein SEQ ID NOS: 1-21 are compared to the HLA-G and HLA-G linked nucleic acid sequences from at least one member selected from the group consisting of a female, a male, and a fetus.

69. The test kit of claim 67, wherein the HLA-G and HLA-G linked nucleic acid sequences from one or more of the group consisting of a female, a male, and a fetus, is analyzed for one or more of:

(a) the C allele or the T allele of codon 93 in exon 3; and

(c) the Insertion allele or the Deletion allele of exon 8.

70. The test kit of claim 69, wherein all or part of any HLA-G sequence and/or HLA-G linked sequences is amplified.

71. The test kit of claim 70, wherein amplification is performed by a method or combination of methods selected from the polymerase chain reaction, nucleic acid sequence based amplification, self sustained sequence replication, transcription-mediated amplification, strand displacement amplification, and the ligase chain reaction using primers as identified by SEQ ID NOS: 1, 2, 3, 10, 11, 14 and 15.

REMARKS

Claims 1-26 have been cancelled and new claims 27-71 have been added. Accordingly, after entry of the instant amendment, claims 27-71 will be pending in the instant application. The amendments herein are presented in response to the outstanding (second) restriction requirement, and further in order to clarify and define the subject matter of Applicants' invention. No new matter has been added by virtue of those amendments; support therefor can be found throughout the specification and in the original claims of the application.

As an initial matter, it is noted that Applicants filed a response on November 25, 2002, to an earlier restriction requirement. The present Office Action seeks to further restrict the claims for initial examination and requires an election of one in ten additional groups.